

WE CLAIM:

1. A concentrated antibody composition consisting essentially of an aqueous solution of antibodies and histidine or acetate buffer at a concentration in the range of from about 2 mM to about 48 mM.

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2. The composition of claim 1, wherein the concentration of histidine or acetate buffer is in the range of from about 3 mM to about 48 mM.

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3. The composition of claim 1, wherein the concentration of histidine or acetate buffer is in the range of from about 4 mM to about 45 mM.

4. The composition of claim 1, wherein the concentration of histidine or acetate buffer is in the range of from about 5 mM to about 40 mM.

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5. The composition of claim 1, wherein the concentration of histidine or acetate buffer is in the range of from 20 mM to 25 mM.

6. The composition of claim 1, wherein the pH is in the range of from about 4.0 to about 7.5.

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7. The composition of claim 1, wherein the pH is in the range of from 4.5 to 7.0.

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8. The composition of claim 1, wherein the pH is in the range of from 5.0 to 6.5.

9. The composition of claim 1 that has pH in the range of from 5.5 to 6.0.

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10. The composition of claim 1, wherein the antibodies are monoclonal antibodies.

11. The composition of claim 10, wherein the antibodies are chimeric antibodies comprising variable regions of one species and constant regions of a different species.

12. The composition of claim 11, wherein the antibodies are chimeric antibodies comprising variable regions of a non-human species and human constant regions.

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13. The composition of claim 12, wherein the antibodies are chimeric antibodies comprising variable regions of an Old World monkey and human constant regions.

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14. The composition of claim 10, wherein the antibodies are humanized antibodies comprising hypervariable regions of a non-human species and human constant regions.

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15. The composition of claim 1, wherein the antibodies are of one or more of the isotypes selected from IgG, IgM, IgA, IgD, and IgE.

16. The composition of claim 15, wherein the antibodies are IgG antibodies.

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17. The composition of claim 16, wherein the antibodies are IgG₁ or IgG₄ antibodies.

18. The composition of claim 1, wherein the concentration of the antibodies is at least 50 mg/ml.

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19. The composition of claim 1, wherein the concentration of the antibodies is at least 100 mg/ml.

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20. The composition of claim 1, wherein the antibodies comprise monoclonal antibodies selected from the group consisting of anti-CD80, anti-gp39, anti-CD4, anti-CD23, and anti-CD20 antibodies.

21. The composition of claim 20, wherein the antibodies comprise at least one monoclonal antibody selected from the group consisting the anti-CD80 antibody IDEC-

114, the anti-gp39 antibody IDEC-131, the anti-CD4 antibody IDEC 151, the anti-CD23 antibody IDEC-152, and the anti-CD20 antibody RITUXAN®.

22. A method for producing a concentrated antibody preparation comprising
5 the steps of:

a) providing an initial antibody preparation consisting essentially an aqueous solution of antibodies and histidine or acetate buffer at a concentration in the range of from about 2 mM to about 48 mM; and

b) subjecting the initial antibody preparation to membrane filtration that
10 removes water and buffer but not antibodies from the antibody preparation,

thereby producing an antibody preparation having a higher concentration of antibodies than the initial antibody preparation.

23. The method of claim 22, wherein the concentration of histidine or acetate
15 buffer in the initial antibody preparation is in the range of from about 3 mM to about 48 mM.

24. The method of claim 22, wherein the concentration of histidine or acetate
20 buffer in the initial antibody preparation is in the range of from about 4 mM to about 45 mM.

25. The method of claim 22, wherein the concentration of histidine or acetate
25 buffer in the initial antibody preparation is in the range of from about 5 mM to about 40 mM.

26. The method of claim 22, wherein the concentration of histidine or acetate
buffer in the initial antibody preparation is in the range of from 20 mM to 25 mM.

27. The method of claim 22, wherein the pH of the initial antibody preparation
30 is in the range of from about 4.0 to 7.5.

28. The method of claim 22, wherein the pH of the initial antibody preparation
is in the range of from 4.5 to 7.0.

29. The method of claim 22, wherein the pH of the initial antibody preparation is in the range of from 5.0 to 6.5.

5 30. The method of claim 22, wherein the pH of the initial antibody preparation is in the range of from 5.5 to 6.0.

31. The method of claim 22, wherein the antibodies are monoclonal antibodies.

10 32. The method of claim 31, wherein the antibodies are chimeric antibodies comprising variable regions of a non-human species and human constant regions.

33. The method of claim 32, wherein the antibodies are chimeric antibodies comprising variable regions of an Old World monkey and human constant regions.

15 34. The method of claim 31, wherein the antibodies are humanized antibodies comprising hypervariable regions of a non-human species, at least one human framework region and human constant regions.

20 35. The method of claim 22, wherein the antibodies are of one or more of the isotypes selected from IgG, IgM, IgA, IgD, and IgE.

36. The method of claim 35, wherein the antibodies are IgG antibodies.

25 37. The method of claim 36, wherein the antibodies are IgG₁ or IgG₄ antibodies.

38. The method of claim 22, wherein the concentration of the antibodies in the antibody preparation produced by step b) is at least 50 mg/ml.

30 39. The method of claim 22, wherein the concentration of the antibodies in the antibody preparation produced by step b) is at least 100 mg/ml.

40. The method of claim 22, wherein the antibodies comprise monoclonal antibodies selected from the group consisting of anti-CD80, anti-gp39, anti-CD4, anti-CD23, and anti-CD20 antibodies.

5 41. The method of claim 22, wherein the antibodies comprise at least one monoclonal antibody selected from the group consisting the anti-CD80 antibody IDEC-114, the anti-gp39 antibody IDEC-131, the anti-CD4 antibody IDEC 151, the anti-CD23 antibody IDEC-152, and the anti-CD20 antibody rituximab.

10 42. An improved method for producing a concentrated antibody preparation comprising the steps of:

a) providing an initial antibody preparation consisting essentially of an aqueous solution of antibodies and buffer; and

b) subjecting the initial antibody preparation to membrane filtration that
15 removes water and buffer but not the antibodies from the antibody preparation,

thereby producing an antibody preparation having a higher concentration of antibodies than the initial antibody preparation;

the improvement consisting of using buffer selected from histidine or acetate at a concentration in the range of from about 2 mM to about 48 mM.

20 43. The improved method of claim 42, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from about 3 mM to about 48 mM.

25 44. The improved method of claim 42, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from about 4 mM to about 45 mM.

30 45. The improved method of claim 42, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from about 5 mM to about 40 mM.

46. The improved method of claim 42, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from 20 mM to 25 mM.

5 47. The improved method of claim 42, wherein the pH of the initial antibody preparation is in the range of from about 4.0 to 7.5.

48. The improved method of claim 42, wherein the pH of the initial antibody preparation is in the range of from 4.5 to 7.0.

10 49. The improved method of claim 42, wherein the pH of the initial antibody preparation is in the range of from 5.0 to 6.5.

15 50. The improved method of claim 42, wherein the pH of the initial antibody preparation is in the range of from 5.5 to 6.0.

51. The improved method of claim 42, wherein the antibodies are monoclonal antibodies.

20 52. The improved method of claim 51, wherein the antibodies are chimeric antibodies comprising variable regions of a non-human species and human constant regions.

25 53. The improved method of claim 52, wherein the antibodies are chimeric antibodies comprising variable regions of an Old World monkey and human constant regions.

30 54. The improved method of claim 51, wherein the antibodies are humanized antibodies comprising hypervariable regions of a non-human species, at least one human framework region and human constant regions.

55. The improved method of claim 42, wherein the antibodies are of one or more of the isotypes selected from IgG, IgM, IgA, IgD, and IgE.

56. The improved method of claim 55, wherein the antibodies are IgG antibodies.

57. The improved method of claim 56, wherein the antibodies are IgG₁ or IgG₄ antibodies.

58. The improved method of claim 42, wherein the concentration of the antibodies in the antibody preparation produced by step b) is at least 50 mg/ml.

59. The improved method of claim 42, wherein the concentration of the antibodies in the antibody preparation produced by step b) is at least 100 mg/ml.

60. The improved method of claim 42, wherein the antibodies comprise monoclonal antibodies selected from the group consisting of anti-CD80, anti-gp39, anti-CD4, anti-CD23, and anti-CD20 antibodies.

61. The improved method of claim 42, wherein the antibodies comprise at least one monoclonal antibody selected from the group consisting the anti-CD80 antibody IDEC-114, the anti-gp39 antibody IDEC-131, the anti-CD4 antibody IDEC 151, the anti-CD23 antibody IDEC-152, and the anti-CD20 antibody rituximab.

62. A method for producing a pharmaceutical composition comprising antibodies as the active ingredient, comprising the steps of:

a) providing an initial antibody preparation consisting essentially of an aqueous solution of antibodies and histidine or acetate buffer at a concentration in the range of from about 2 mM to about 48 mM; and

b) subjecting the initial antibody preparation to membrane filtration that removes water and buffer but not antibodies from the antibody preparation, thereby producing an antibody preparation having a higher concentration of antibodies than the initial antibody preparation; and

c) combining the concentrated antibody preparation of step b) with one or more pharmaceutically acceptable carriers to produce a pharmaceutical composition.

63. The method of claim 62, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from about 3 mM to about 48 mM.

5 64. The method of claim 62, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from about 4 mM to about 45 mM.

10 65. The method of claim 62, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from about 5 mM to about 40 mM.

66. The method of claim 62, wherein the concentration of histidine or acetate buffer in the initial antibody preparation is in the range of from 20 mM to 25 mM.

15 67. The method of claim 62, wherein the pH of the initial antibody preparation is in the range of from about 4.0 to 7.5.

20 68. The method of claim 62, wherein the pH of the initial antibody preparation is in the range of from 4.5 to 7.0.

69. The method of claim 62, wherein the pH of the initial antibody preparation is in the range of from 5.0 to 6.5.

25 70. The method of claim 62, wherein the pH of the initial antibody preparation is in the range of from 5.5 to 6.0.

71. The method of claim 62, wherein the antibodies are monoclonal antibodies.

30 72. The method of claim 71, wherein the antibodies are chimeric antibodies comprising variable regions of a non-human species and human constant regions.

73. The method of claim 72, wherein the antibodies are chimeric antibodies comprising variable regions of an Old World monkey and human constant regions.

74. The method of claim 71, wherein the antibodies are humanized antibodies comprising hypervariable regions of a non-human species, at least one human framework region and human constant regions.

5 75. The method of claim 62, wherein the antibodies are of one or more of the isotypes selected from IgG, IgM, IgA, IgD, and IgE.

76. The method of claim 75, wherein the antibodies are IgG antibodies.

10 77. The method of claim 76, wherein the antibodies are IgG₁ or IgG₄ antibodies.

15 78. The method of claim 62, wherein the concentration of the antibodies in the antibody preparation produced by step b) is at least 50 mg/ml.

79. The method of claim 62, wherein the concentration of the antibodies in the antibody preparation produced by step b) is at least 100 mg/ml.

20 80. The method of claim 62, wherein the antibodies comprise monoclonal antibodies selected from the group consisting of anti-CD80, anti-gp39, anti-CD4, anti-CD23, and anti-CD20 antibodies.

25 81. The method of claim 62, wherein the antibodies comprise at least one monoclonal antibody selected from the group consisting the anti-CD80 antibody IDEC-114, the anti-gp39 antibody IDEC-131, the anti-CD4 antibody IDEC 151, the anti-CD23 antibody IDEC-152, and the anti-CD20 antibody rituximab.

30 82. An improved method of therapy that includes the administration of a pharmaceutical composition comprising an antibody, the improvement comprising administering a pharmaceutical composition that is made by combining

a) an antibody preparation consisting essentially of an aqueous solution containing at least one therapeutically effective dose of an antibody and histidine or

acetate buffer at a concentration in the range of from about 2 mM to about 48 mM that has been concentrated by membrane filtration, and

b) one or more pharmaceutically acceptable carriers to produce a pharmaceutical composition.

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83. The improved method of claim 82, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from about 3 mM to about 48 mM.

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84. The improved method of claim 82, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from about 4 mM to about 45 mM.

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85. The improved method of claim 82, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from about 5 mM to about 40 mM.

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86. The improved method of claim 82, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from 20 mM to 25 mM.

87. The improved method of claim 82, wherein the pH of the antibody preparation of a) is in the range of from about 4.0 to 7.5.

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88. The improved method of claim 82, wherein the pH of the antibody preparation of a) is in the range of from 4.5 to 7.0.

89. The improved method of claim 82, wherein the pH of the antibody preparation of a) is in the range of from 5.0 to 6.5.

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90. The improved method of claim 82, wherein the pH of the antibody preparation of a) is in the range of from 5.5 to 6.0.

91. The improved method of claim 82, wherein the antibodies are monoclonal antibodies.

92. The improved method of claim 91, wherein the antibodies are chimeric antibodies.

93. The improved method of claim 91, wherein the antibodies are humanized antibodies.

94. The improved method of claim 82, wherein the antibody preparation of a) comprises antibodies that are of one or more of the isotypes selected from IgG, IgM, IgA, IgD, and IgE.

95. The improved method of claim 94, wherein the antibodies are IgG antibodies.

96. The improved method of claim 95, wherein the antibodies are IgG₁ or IgG₄ antibodies.

97. The improved method of claim 82, wherein the concentration of the antibodies in the antibody preparation of a) is at least 50 mg/ml.

98. The improved method of claim 82, wherein the concentration of the antibodies in the antibody preparation of a) is at least 100 mg/ml.

99. The improved method of claim 82, wherein the antibodies comprise monoclonal antibodies selected from the group consisting of anti-CD80, anti-gp39, anti-CD4, anti-CD23, and anti-CD20 antibodies.

100. The improved method of claim 82, wherein the antibodies comprise at least one monoclonal antibody selected from the group consisting the anti-CD80 antibody IDEC-114, the anti-gp39 antibody IDEC-131, the anti-CD4 antibody IDEC 151, the anti-CD23 antibody IDEC-152, and the anti-CD20 antibody rituximab.

101. The improved method of claim 82, comprising administering a therapeutically effective dose of therapeutic antibody to a patient suffering from a disease selected from the group consisting of cancer, allergic disorders, autoimmune diseases, and lymphoma.

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102. A kit useful for the treatment of a mammal suffering from or predisposed to a disorder comprising

at least one container containing a pharmaceutical composition that is the product of combining:

10 a) an antibody preparation consisting essentially of an aqueous solution containing at least one therapeutically effective dose of an antibody and histidine or acetate buffer at a concentration in the range of from about 2 mM to about 48 mM that has been concentrated by membrane filtration, and

b) one or more pharmaceutically acceptable carriers;

15 and further comprises a label or an insert indicating that said pharmaceutical composition may be used to treat said disorder.

103. The kit of claim 102, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from about 3 mM to about 48 mM.

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104. The kit of claim 102, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from about 4 mM to about 45 mM.

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105. The kit of claim 102, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from about 5 mM to about 40 mM.

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106. The kit of claim 102, wherein the concentration of histidine or acetate buffer in the antibody preparation of a) is in the range of from 20 mM to 25 mM.

107. The kit of claim 102, wherein the pH of the antibody preparation of a) is in the range of from about 4.0 to 7.5.

108. The kit of claim 102, wherein the pH of the antibody preparation of a) is in the range of from 4.5 to 7.0.

5 109. The kit of claim 102, wherein the pH of the antibody preparation of a) is in the range of from 5.0 to 6.5.

110. The kit of claim 102, wherein the pH of the antibody preparation of a) is in the range of from 5.5 to 6.0.

10 111. The kit of claim 102, wherein the antibodies are monoclonal antibodies.

112. The kit of claim 111, wherein the antibodies are chimeric antibodies.

15 113. The kit of claim 111, wherein the antibodies are humanized antibodies.

114. The kit of claim 102, wherein the antibody preparation of a) comprises antibodies that are of one or more of the isotypes selected from IgG, IgM, IgA, IgD, and IgE.

20 115. The kit of claim 114, wherein the antibodies are IgG antibodies.

116. The kit of claim 115, wherein the antibodies are IgG₁ or IgG₄ antibodies.

25 117. The kit of claim 102, wherein the concentration of the antibodies in the concentrated antibody preparation of a) is at least 50 mg/ml.

118. The kit of claim 102, wherein the concentration of the antibodies in the concentrated antibody preparation of a) is at least 100 mg/ml.

30 119. The kit of claim 102, wherein the antibodies comprise monoclonal antibodies selected from the group consisting of anti-CD80, anti-gp39, anti-CD4, anti-CD23, and anti-CD20 antibodies.

120. The kit of claim 102, wherein the antibodies comprise at least one monoclonal antibody selected from the group consisting the anti-CD80 antibody IDEC-114, the anti-gp39 antibody IDEC-131, the anti-CD4 antibody IDEC 151, the anti-CD23 antibody IDEC-152, and the anti-CD20 antibody rituximab.

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121. The kit of claim 102, which is useful for treating a disorder selected from the group consisting of cancer, allergic disorders, autoimmune diseases, and lymphoma.